Challengeability of biotechnology patents in the light of Biogen v. Medeva

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On 27 October 1994, the English Court of Appeal overturned the previously successful defence of Biogen's patent concerning the production of hepatitis B viral antigens using recombinant DNA technology. On 15 May 1995, Biogen was granted leave to appeal to the highest court in the UK, the House of Lords. The case of Biogen v. Medeva considered a number of key areas including obviousness, insufficiency and width of patent claims and will have a major impact in the field of biotechnology patents. This article considers some of the issues relating to obviousness and insufficiency that will need to be considered afresh by the House of Lords.

A patent is a monopoly granted by a government to an inventor, in return for disclosure of his invention to the public. In general, it lasts for 20 years (extendable by up to 5 years, for certain pharmaceutical inventions) and operates as an exclusive right to use the invention and to prevent others from doing so without a licence.

Patent criteria

It has been said that patentable subject matter includes 'anything under the sun that is made by man' whether living or not[1].

However, for an invention to be patentable in the UK it must be:

- novel
- inventive (i.e. not obvious)
- capable of industrial application
- not excluded by statute (i.e. it should consist of patentable subject matter)

These criteria apply to all inventions, including those in the fields of biotechnology and gene therapy. Similar criteria apply in many countries and, whilst the Biogen v. Medeva case is specifically concerned with English and (now it is before the House of Lords) UK law, the issues discussed here may be applicable in a much wider context, as shown by the references in this article to cases decided before the European Patent Office (EPO).

The granting of a patent by a Patent Office is no guarantee that it was done so validly. Hence the patent can be revoked if expert evidence reveals that the invention was not 'new' or not 'inventive' at the time the application for the patent was made or that the patent does not contain a sufficient description of the invention.

The case of Biogen v. Medeva

In the late 1970s, the hepatitis B virus (HBV) was known and its constituents partially characterized. A vaccine was unobtainable by conventional means, however, because the only effective agent capable of stimulating the immune system at the time was the 'live' virus itself. Biogen used recombinant techniques, which were at an early stage of development, to

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produce antigens that would bind to antibodies against HBV and, it was hoped, act as a vaccine and stimulate the production of neutralizing antibodies. In 1978 and 1979, Biogen applied for patents which were granted in 1990 for both surface and core proteins and their expresssion in bacterial, yeast and mammalian host cells. These patents also covered DNA molecules coding for both surface and core antigens. When Medeva announced plans to market an HBV vaccine, Biogen took them to court, claiming infringement of their patents. In the English High Court, the Judge found Biogen's main patent was valid and had been infringed by Medeva's vaccine. The defendants appealed to the English Court of Appeal[2] and were successful in challenging the original judgment. On 15 May 1995 the Appeal Committee of the House of Lords gave Biogen leave to appeal against the judgment of the Court of Appeal and therefore the issue of the UK patent's validity will be considered afresh by the full panel of the House of Lords sometime next year.

The issues of obviousness and sufficiency, the two principal criteria under which biotechnology patents are often attacked, are central in this case.

Obviousness

To be patentable an invention must contain an inventive step. English courts have struggled to define inventiveness and rely heavily on expert evidence as to whether particular steps would have been obvious to a researcher in that particular field at the time the patent is applied for.

Generally, an invention is only obvious if the 'man skilled in the art' would have thought the idea 'worth trying' or that he had 'a reasonable expectation of success'. The EPO however, regards inventions that solve a particular technical problem in the field as satisfying the requirement for an inventive step. This roughly equates with the UK doctrine of 'long felt want': if an invention enjoys commercial success there is an implication that researchers had long been looking for a solution to a particular problem and thus the invention, which solves the problem, must have been 'inventive'.

Recent case law on the issue of inventiveness with respect to biotechnological inventions is confused. Many patent applications for gene cloning were filed in the 1980s with claims for 'recombinant or isolated DNA encoding protein X'. Now that the techniques involved have become easier and more predictable, these claims, arguably, are less 'inventive'.

For example, in Genentech's patent for human growth hormone[3], it was held that it was inventive to make a DNA vector insert that lacked the DNA sequence coding for the protein's signal polypeptide because this was applying known DNA recombinant techniques in a nonobvious way. Similarly, in the recent case of Chiron v. Organon[4], which involved recombinantly produced hepatitis C viral polypeptides and their use, amongst others, in diagnostic kits, the Court held:

> The work done by Chiron was *unique*. Nobody before had identified a virus where the antigen had not been identified, and no antibody : antigen response had been established even though *the techniques employed were well known at the time* (emphasis added).

By way of contrast, in relation to Genentech's patent[5] on recombinant human tissue plasminogen activator (tPA), it was held by the English Court of Appeal that the patent was invalid because it would have been obvious to try to produce human tPA by recombinant DNA technology: all the steps taken to elicit the relevant DNA sequences and then application of the knowledge of such sequences to produce human tPA were considered to be mere applications of known technology with no originality. The fact that an enormous amount of work had been involved was of no relevance to the inventiveness issue. As Lord Justice Mustill (one of the three judges hearing the case) put it: "First to the post is the test of novelty, but novelty is not enough."

In the case Biogen v. Medeva[2], the English Court of Appeal reverts to the thinking behind Genentech's tPA patent[5] rather than following the more recent case of Chiron v. Organon[4]. Biogen's patent concerned the production of hepatitis B viral antigens using recombinant DNA technology. At the time of this invention, most researchers considered it technically impossible, not least because it was thought that the presence of introns would have prevented successful expression of the proteins. However, the Court of Appeal held that even though Biogen were:

> prepared to make the necessary investment of time and money.... This is not a description of an inventive step. Nothing the Plaintiffs did was not obvious if you took the business decision to do it. Others considered the odds against success too long to justify trying.

This is in direct contrast to the EPO Technical Board of Appeal's conclusion that Biogen's equivalent European patent was valid. They commented[6]:

> The successful achievement of HBV genes in a recombinant DNA system regardless of whether it was just a 'lucky strike' or as a result of 'looking for the unexpected' or of a planned strategy was a major breakthrough in HBV research.

If the House of Lords ultimately endorses the Court of Appeal's decision in the case of Biogen v. Medeva, the effects on existing and future biotechnology patents will be far reaching.

The principles of recombinant DNA technology are well known and if use of such established methodology is to be considered non-inventive (where the technology is used to produced a known product), then the chances of obtaining patents for such biotechnological inventions in the UK will be extremely limited, although they are likely to remain patentable in the rest of Europe and elsewhere.

Insufficiency

The second principal criterion under which a patent is usually attacked is that of insufficiency. An invention will be declared invalid if 'the specification does not disclose the invention clearly enough and completely enough for it to be performed by a person skilled in the art'[7].

In the English Court of Appeal case of Mentor Corporation v. Hollister Inc.[8], Mentor was owner of a patent for a male incontinence device, and was claiming Hollister had infringed its patent by marketing a similar product without its consent. Lord Justice Lloyd, who read out the judgment, commented that:

> Disclosure of an invention does not have to be complete in every detail, so that anyone whether skilled or not, can perform it...

Although the Court realized there will be difficulties in drawing the line between sufficient and insufficent disclosures, Lord Justice Lloyd went on to say that:

> If there are actual errors in the specification – if the apparatus really will not work without departing from what is described – then, unless both the existence of the error and the way to correct it can be quickly discovered by the addressee of the degree of skill and knowledge which we envisage, the description is insufficient.

But what about broad claims? Patent agents draft claims as widely as possible in order to broaden the scope of the monopoly so that as many variants of the invention are covered as possible. However, the patent specification itself will commonly only disclose how to work some of these variants. But do broad claims satisfy the requirement for sufficient disclosure if the specification describes the invention with respect to only a few variants? What if, for instance, the examples in the specification are not repeatable with 100% certainty? The EPO Technical Board of Appeal has held an invention to be sufficiently disclosed if:

> at least one way is clearly indicated, enabling the skilled person to carry out the invention. [Indeed,] the disclosure need not include specific instructions as to how all possible component variants within the functional definition should be obtained.

This was confirmed in the case of Molnlyke AB v. Procter & Gamble Ltd[9], which concerned the infringement of a patent for an improved refastenable disposable diaper. The Judge in that case, Mr Justice Morritt, observed:

> [The Act] does not set a standard whereby the man skilled in the art must be able to make all possible embodiments. But he must be able to make an embodiment using the information disclosed in the specification, his common general knowledge and any normal and reasonable trial and error.

The EPO Technical Board of Appeal went further in the case of Biogen/Alpha Interferons[10], in which several other companies were opposing Biogen's application to the EPO for a patent relating to recombinant human alpha interferons. It held:

> there is no necessity to provide instructions and advance how each and every member of the class would have to be prepared. In view of the nature of the technique, there is not even a guarantee the same product is obtained from the same source after an identical repetition of the complicated and lengthy experiments.

Yet in the case of Exxon/Fuel Oils[11], where Exxon were appealing against a decision by the EPO to refuse their application for a patent for a new method of treating fuel oils to give them better low temperature handling characteristics, the Board of Appeal set a limit to what had become known as the 'one-way rule' in that:

> the disclosure of one way of performing the invention is only sufficient within the meaning of [the sufficiency requirement] if it allows the person skilled in the art to perform the invention in the whole range that is claimed.

It was this decision that provided the English Court of Appeal with the basis for their finding in Biogen v. Medeva[2] that the patent in question was 'insufficent'. In this case, the patent claimed to cover, in effect, four inventions: expression of both core and surface hepatitis B viral antigens in both bacterial and non-bacterial hosts. However, at the time the patent was claimed Biogen had only succeeded in expressing viral surface antigen in *Escherichia coli*. This meant that they could only disclose expression in one host in the patent specification. The Court of Appeal held that the patent was invalid because:

> The disclosure must be sufficient to enable the whole width of the claimed invention to be performed. What will suffice to satisfy this criterion will vary depending on the nature of the claim that has been made... It is not the law that the disclosure of a single embodiment will always satisfy the requirement regardless of the width of the claim.

Hence, if a claim is drafted broadly there is now a co-relative obligation to make a correspondingly broad disclosure.

If this remains the law following Biogen's appeal to the House of Lords, it could have major implications for existing biotechnological patents, many of which also contain broad claims. A large number of them could be declared invalid on the grounds of insufficiency. Presumably the thinking behind the Biogen decision[2] is to try to avoid the situation where a patentee refuses to grant a licence for his invention which, if the patent covers all conceivable hosts, would prevent third parties from developing a successful variant. Understandably, the patentee will wish to recoup his investment with a return on his own product, but this must be balanced against the public interest of having an improved second-generation pharmaceutical product on the market as soon as possible. UK patent law does provide for the grant of compulsory licences if the patentee abuses his monopoly, for example, by refusing to licence the invention, or doing so but under unreasonable terms. This provision, however, is seldom invoked.

A consequence of the Biogen decision as it stands at the moment is that, if a patentee is only entitled to claim expression in the host disclosed in the specification, it will be all too easy for rival companies to avoid infringement by producing the given protein in a new, more recently developed host. This would render most, if not all, UK patents in this field effectively worthless. Patents granted by the EPO and other patent offices elsewhere would be unaffected by this decision. However, this is an unsatisfactory position so far as the UK is concerned and will result in an inconsistent approach with regard to patents in this field. The decision of the House of Lords is awaited with much interest by industry and patent professionals.

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